II. Summary of Interview

Applicants wish to thank the Examiner, her Primary Examiner, and her Supervisory Primary Examiner for the courtesy of the personal interview of April 16, 2002. At the interview, counsel for Applicants pointed out that the new matter rejection did not comport with prevailing decisional law. The Examiner expressed a willingness to discuss this issue with Quality Assurance Specialist, Mr. Robert Hill.

Counsel further pointed out that the lack of enablement rejection under 35 U.S.C. § 112, first paragraph was based in part improperly on the unsupported personal opinion of the Examiner, that working examples in the specification were not necessary, and that dosages could be readily determined by one skilled in the art. Counsel noted that the fact that the parent application was abandoned did not change the fact that the declaration evidence submitted in the parent was apparently sufficient to overcome an identical lack of enablement rejection therein. The Examiner noted she was not bound by the decision of another Examiner, but she expressed a willingness to discuss the case with the previous Examiner. In addition, the Examiner furnished Applicants' representatives with a reference, which she thought supported her position. This reference is discussed below as part of Applicants' remarks.

Finally, the Examiner suggested some claims that could avoid a lack of enablement rejection. Applicants thank the Examiner for her suggestion. These claims have been newly presented above.

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II. Rejections Under 35 U.S.C. § 112, First Paragraph

Enablement Rejection

Claims 28-33 were again rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to provide an enabling disclosure. Applicants respectfully traverse this rejection.

The Examiner has found insufficient the declaration by Professor Colin L. Masters filed under 37 C.F.R. § 1.132 in parent application number 08/757,537. She stated, "the initial elevation of APP *might* just as well be a part of normal response to elevated concentration of zinc and in fact *may* be the beginning of a process of damage repair, which is a normal function of APP." Final Office Action at page 3 (emphasis added.) Applicants respectfully submit that the Examiner has applied an improper standard of evaluation of the evidence of record.

Applicants' disclosure is presumptively enabled. The Examiner may not substitute her own personal opinion, unsupported by evidence, to rebut the presumption of enablement. See MPEP § 2164.05. At the personal interview of April 16, 2002, the Examiner referred to a paper by Jean Constantinidis, *Drug Development Research* 27:1-14 (1992). This paper appears to be a sequel to the Constantinidis paper cited previously by Applicants in their Information Disclosure Statement filed April 19,2001. The Examiner relied on this paper as evidence of contradictory theories regarding the role of zinc in the treatment of Alzheimer's disease. Constantinidis found amyloid-induced deficiency in hippocampal zinc in patients with Alzheimer's disease, and advocated treatment with zinc aspartate to correct any such deficiency.

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Applicants submit that the Constantinidis paper is not inconsistent with their disclosure. As noted on page 6 of Applicants' specification, extracellular zinc modulates the expression of amyloid precursor protein (APP.) Applicants have found that high zinc levels also play a role in promoting aberrant proteolytic processing of APP into amyloid protein. Specification at pages 7-8. It follows that if zinc plays a role in producing elevated levels of APP and in the proteolytic processing of APP, zinc would be consumed, so that lower zinc levels would be expected in Alzheimer's patients. Furthermore, it is now known that the plaques that form in the brain as a result of the elevated levels of APP and the aberrant proteolytic processing of APP are able to sequester zinc, leading to an expectation that there would be lower levels of zinc in areas of the brain other than plaque. Accordingly, the Office is requested to withdraw this ground of rejection.

The Examiner has maintained her requirement for working examples. Applicants submit that one skilled in the art could readily practice the instant invention without the need for working examples. Disappearance of the symptoms of Alzheimer's disease would be readily observable and indicative of efficacy. Furthermore, the Examiner is reminded that all the evidence of record, not just the specification as filed, must be evaluated in a proper determination of enablement. Such evidence would include factual declarations under 37 C.F.R. § 1.132 or references. MPEP § 2164.05. Some of the evidence in the declaration under 37 C.F.R. § 1.132 by Professor Masters is in the form of working examples. Therefore, Applicants submit that working examples are in fact of record. The Examiner in the parent application apparently considered all of the

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evidence of record and found it sufficient to overcome the identical issue. The fact that the parent application is abandoned does not alter this fact. Final Office Action at page 4.

The Examiner has agreed that the TG2576 mouse model is an accepted model for the treatment of Alzheimer's disease, but she argues that the art recognizes limitations of that model. Final Office Action at page 4. The Examiner's argument focuses on how the mice developed their Aß brain deposits. Applicants submit that this fact is irrelevant to the subsequent use of the mice as models for Alzheimer's disease. All that is important for Applicants' use of the mice is that they have brain deposits, not how the deposits got there. Note that Professor Masters used the mice in a behavioral test, and he observed cessation of movements typical of diseased mice after treatment.

Finally, the Examiner has maintained her position that dosages must be disclosed in Applicants' specification. Final Office Action at page 5. Applicants submit that one skilled in the art could readily practice the instant invention without a disclosure of specific dosages. Undue experimentation would not be required to determine effective dosages in an acceptable model and to extrapolate those dosages for humans. As noted above, the TG2576 mouse model is a recognized model for studying Alzheimer's disease. Furthermore, the Examiner again has failed to consider all of the evidence of record, and she has focused only on the specification as filed. There are numerous references of record directed toward the pharmaceutical treatment of humans with Alzheimer's disease. Applicants' submit that given these references, one skilled in the art could readily determine appropriate dosages for the agents employed in their claimed methods. Withdrawal of all aspects of this rejection is requested.

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New Matter Rejection

The Examiner has rejected claims 28-33 as lacking adequate support or written description for the proviso added to claim 28 by the amendment of December 10, 2001. Final Office Action at page 6. Applicants respectfully traverse this rejection.

The decisional law is settled in this area. See *In re Johnson and Farnham*, 194 U.S.P.Q. 187, 196 (CCPA 1977). The work of another may be excised from a claim so long as the written description supports the amended claim that includes the limitation. The proviso is merely the vehicle by which Applicants have excised EDTA. EDTA was disclosed in Applicants' specification as filed. See Specification at page 9, line 10. Applicants are free to claim or not to claim that which is disclosed in their specification. Here they have chosen not to claim EDTA. No new matter has been introduced by their choice or the manner in which they have claimed it. Withdrawal of this rejection is requested.

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CONCLUSION

Applicants respectfully request entry of the amendments, reconsideration and reexamination of this application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: May 20, 2002

By: _____ FOR
Charles E. Van Horn
Reg. No. 40,266

342094

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